showed little effects of target uncertainty. An obvious question in studies with such small sample sizes is whether or not the sampled responses reflect the population as a whole. If so, does this imply that there could be small sub-populations of caudate neurons that signal target uncertainty? Or was that selectivity just a chance occurrence? If not, what is the selectivity of most caudate neurons? What other factors affect their responses? Indeed, other response properties have been found in the caudate, including a suppression of responses in anticipation of an eye movement to a rewarded location [7] and a representation of color-reward contingencies [6]. Learning how these different properties are represented across the population of neurons in the caudate will be an essential step in understanding its role in using information related to reward to influence oculomotor behavior.

Conclusions

The fact that an expectation of reward can strongly bias our decisions and actions – especially, as Paris and I can attest to personally, if the reward involves marrying the most beautiful woman in the world – is not in dispute. What is uncertain is exactly how brain links signals related to reward expectation [3] to the signals responsible for making decisions and preparing actions [15]. Several recent studies have characterized the influence of reward expectation on neural circuits involved in sensory–motor transformations [14,16–20]. The study by Lauwereyns and colleagues [4] adds to that short list and provides novel insights into how the brain might use signals related to a spatially selective anticipation of reward to bias a simple oculomotor behavior. It will be interesting to see whether the same principles can be extended to include other factors and more complex behaviors.

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A prominent role for intrinsic neuronal properties in temporal coding

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A recent report presents evidence that the exact timing of action potential output in rat hippocampal pyramidal neurons is similarly modulated during several diverse forms of behavior. These data suggest that it is, to a large degree, the intrinsic properties of the neurons themselves that produce this temporal coding of information. Thus, this report provides an outstanding example of the importance of single neuronal properties, even during complex behaviors.

Hippocampal theta rhythm is a low frequency (5–10 Hz) oscillation of extracellular current that results from the collective activity of groups of neurons ([1]; reviewed in Refs [2–4]). This network oscillation occurs during a wide variety of spatial and non-spatial behaviors and can be thought of as a type of timing signal, upon which the action

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potential firing of single neurons can be referenced. During spatial behaviors, such as a rat navigating through a linear track or an open field, particular neurons within the hippocampus will fire in specific regions of the environment. When the animal is approaching this specific region or 'place field', the neuron in question will increase its firing rate and the timing of the spikes will shift to an earlier time or phase of the theta oscillation (this is known as phase precession) [5–7] (Fig. 1). In contrast to the firing rate, which increases and then decreases as the rat moves through the place field, the shift in spike timing is unidirectional with output always occurring progressively earlier in the theta oscillation [1,6–8]. Phase precession is a well-described phenomenon for spatial behaviors and it is thought to represent one of the clearer examples of temporal coding in the mammalian CNS [9–12]. Furthermore, the unidirectionality of the phase shift, among other things, suggests that this temporal coding could be even more reliable as a predictor of the position of an animal than is the biphasic rate code produced by the place cells [1,8]. However, whether hippocampal neurons encode information using spike timing alone or use it in addition to spike rate is still an open question.

Although phase precession has repeatedly been shown to occur during spatially related behaviors, the Buzsaki group has taken this one step further by recently showing that it also occurs during non-spatial behaviors, such as wheel-running and rapid eye movement (REM) sleep [1,13]. They have now additionally demonstrated that this non-spatial advancement is unidirectional, with spikes occurring at earlier phases during the cessation of firing than during the onset [1]. These observations are particularly important because they indicate that phase precession is a more general feature of hippocampal neurons occurring as the result of a fundamental, perhaps cellular-level, mechanism.

Mechanisms of phase precession

Along these lines, the report of Harris *et al.* also provides some insight into the mechanisms of phase precession. One prominent theory holds that phase precession is produced by an interaction between rhythmic dendritic excitation and somatic inhibition [14–16]. As a rat moves towards the center of the place field, dendritic excitatory input increases and somatic inhibition becomes progressively overwhelmed, causing the neuron to fire more action potentials sooner in the theta phase. In this scheme, in which there are small amounts of excitatory input, the neuron is most likely to fire when it is least inhibited, which is during the positive theta phase. Conversely, when excitatory input is highest, firing will shift towards when the neuron is receiving the most excitation (Fig. 2). Thus, spike firing will advance from the positive to the negative theta phases during a large increase in excitatory input. Data presented by Harris *et al.* show that mean spike phase depended on both spike rate and its temporal derivative, indicating that phase precession occurs only when neurons are firing at relatively elevated rates (~8 Hz and higher). These observations support the above hypothesis that firing phase is a function of

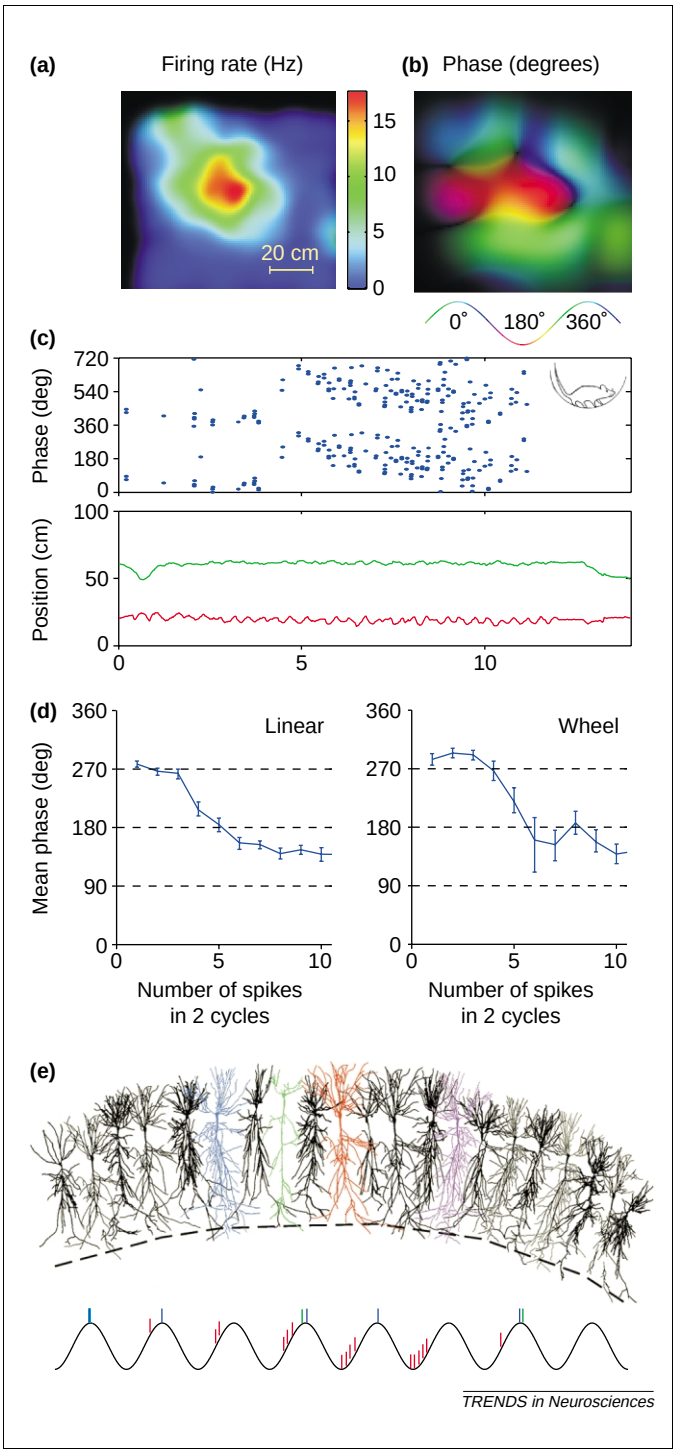

Fig. 1. Action potential firing rate and theta-relative phase in hippocampal pyramidal cells. (a) In what is thought to be an analogous situation to receptive fields of sensory neurons, certain neurons within the hippocampus increase their firing rate when the animal enters specific regions of the environment. A 'place map' is formed by plotting mean firing rate of a representative CA1 pyramidal neuron as a function of position. Vertical scale shows different colors used to denote firing rate in Hz. Scale bar, 20 cm. (b) A 'phase map' of the same cell, produced by plotting mean firing phase (timing of the action potential relative to the theta phase) as a function of the position of the animal. (c) Spike phase advancement during a wheel running episode. Plot of spike phase versus trial time, showing that phase precession occurred even though the head of the rat remained stationary. (d) The relationship of spike rate to phase during a spatial behavior (linear track running) and a non-spatial behavior (wheel running). Phase 0 corresponds to the positive peak of CA1 pyramidal layer theta rhythm. (e) Illustration of the spike-phase relationship for strongly (red) and weakly activated (blue, green and purple) neurons. The strongly activated neuron discharges on the negative phase of the local extracellular theta rhythm, whereas neurons with only threshold activation discharge on the positive phase. Non-spiking cells are shown in black. Adapted, with permission, from Refs [1,4].

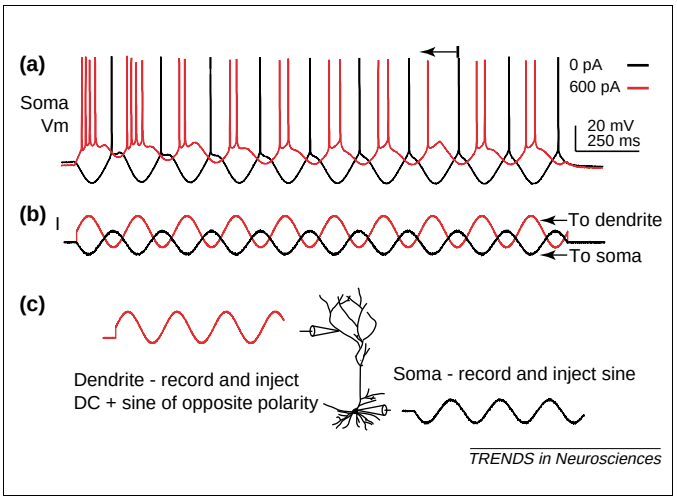

Fig. 2. Phase precession and spike adaptation in CA1 pyramidal neurons located in acute hippocampal slices. (a) The black trace shows somatic membrane potential in response to a 5 Hz sine-wave current injection to the soma alone (200 pA). The red trace shows somatic membrane potential in response to a somatic sine plus 180 degrees out-of-phase sine wave current injection to dendrite (~300 μm; 600 pA). Dendritic current amplitudes are shown at the right of the traces. (b) Current waveforms for somatic (black) and dendritic (red) injections. Both current waveforms were simultaneously injected during generation of the red trace shown in (a). (c) Location of the recording pipettes and the type of current waveform injected. Arrow in (a) shows the phase advancement of spike initiation for increasing-amplitude dendritic currents. Abbreviation: DC, direct current. Adapted, with permission, from Ref. [19].

excitation strength because CA1 neurons usually require an increased excitatory drive to fire at such high rates.

So, if there really is an elevated excitatory drive throughout the movement of the rat through the place field, what causes firing rate to decrease even as firing phase continues to advance? One intriguing idea presented in another paper published in the same issue of *Nature* suggests that total excitatory drive to these cells is actually somewhat asymmetrical after all [8,17]. The asymmetry is produced by the activation of recurrent inhibition and is developed over experience (in this case, repeated laps around a track). Another idea, presented by Harris *et al.*, is that it is the excitability of the individual CA1 pyramidal neurons themselves that decreases during what is essentially a symmetric excitatory input [1]. In this view, even though excitatory input has not decreased, the progressive activation of a K^+ conductance and the resultant spike frequency adaptation cause spike-firing rate to decrease while spike phase continues to advance (Fig. 2). An interesting conjunction of these two ideas would be that both the symmetry of the synaptic input and the excitability of the CA1 pyramidal neurons are changing during experience [18].

At any rate, the observation that, even for non-spatial behaviors, unidirectional phase precession occurs only during times of high excitation adds much to our understanding of the mechanisms of phase precession and points intriguingly towards the fundamental properties of the neurons themselves. That such an important aspect of hippocampal information processing could hinge so tightly on the membrane properties of the individual neurons involved provides a welcome example of the importance of these properties in CNS functions.

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